REMARKS

Claims 132-268 are pending in this application, of which claims 135, 139, 146, 148, 153, 168, 169, 170-172, 178-179, 183 and 196-197 are considered withdrawn as being drawn to a non-elected invention, there being no allowable generic or linking claim. The Office Action presents the following issues: 1) claims 204, 208, and 209 are objected to as being in improper form; 2) non-withdrawn claims 132-134, 136-138, 140-145, 147, 149-152, 154-167, 173-177, 180-182, 184-195 and 198-268 stand rejected under 35 USC §101 as drawn to non-statutory matter; 3) the same non-withdrawn claims stand rejected under 35 USC §112, second paragraph, for failing to particularly point out and distinctly claim the subject matter; 4) claims 132-134, 136-138, 140-145, 147, 149-152, 154-157, 158-161, 162-167, 175, 189-191, 198, 199, 211, 212, 224-226, 250-253 and 258 stand rejected under 35 USC §102(b) in view of Kaufman et al.; 5) claims 132-134, 136-138, 140-144, 150, 159-161, 164-166, 173-177, 180-182, 184-188, 192-195, 200-223 and 227-229 stand rejected under 35 USC §102(e) in view of Galley et al. (US 2003/0028089); 6) claims 132-134, 136-138, 140-145, 147, 149-152, 159-161, 164-166, 173-177, 180-182, 184-188, 192-195, 200-223, 227-229 and 254-268 stand rejected under 35 USC §103(a) in view of Albisser et al. and Ribeiro et al. (US 2003/0055570); and 7) claims 132-134, 136-138, 140-145, 147, 149-152, 154-157, 158-167, 173-177, 180-182, 189-195, 198, 199, 200-229, 250-253 and 258 stand rejected under 35 USC §103(a) in view of Doyle et al. and Galley et al.

Applicants thank the Examiner for the thoroughness of the review of the pending claims particularly in regards to issues 1-3 above. Applicants respectfully request reconsideration of the aforementioned rejections in view of the remarks and amendments presented herein.

1. Claims Objections – Claims 204, 208 and 209

The typographical error in claim 204 and the reference to claim 202 in claim 208 is deleted by the amendments herein, thereby traversing this objection.

2. Claim Rejections – 35 USC §101

The claims under examination stand rejected under §101 for failing to include a step of a physical transformation of matter, or producing a concrete, tangible, and useful result.

In response Applicants have amended the independent claims herein, namely claims, to include a step of producing a concrete, tangible and useful result, thereby traversing this rejection.

3. Claim Rejections – 35 USC §112

Claims 132-134, 136-138, 140-145, 147, 149-152, 154-167, 173-177, 180-182, 184-195 and 198-268 stand rejected under this rejection. Claim 132 has been amended to include adjusting insulin doses delivered or outputted. The claims have also been amended to eliminate the confusion over the use of parentheses, and to address the noted concerns over lack of antecedent basis. A number of the cited claims have also been cancelled to focus the claims on more significant features of Applicants' disclosure. Applicants respectfully submit the concerns raised have now been traversed.

4. Claim Rejections – 35 USC §102(b)

This rejection is based on the article by Kaufman et al. Kaufman et al. disclose a population-based statistically derived fixed formula that does not provide for adjustment of insulin dosing departing from the fixed formula. In contrast, Applicants' disclosure and claims are not directed to a population-statistics based fixed formula. Applicants instead disclose and claim a method that provides for adjustment of insulin dosing based on the particular patient's history without requiring human intervention as discussed in more detail below.

As background, there are several population-based statistically-derived formulas employed in the cited references. Applicants are the developers of two of most widely-used of these formulas. The first of these is a correlation of a Correction Factor (CF) (sometimes called insulin sensitivity) v.s. Total Daily Dose of Insulin (TDD). The correlation follows the model CF = K1 / TDD, where K1 is a constant determined by a statistical correlation. The model itself was developed by Applicant, Dr. Davidson. The value of K1 was originally estimated at 1500, in 1982, based on anecdotal evidence.

It was later estimated by others at 1800, based on Dr. Davidson's model. In 2002 Applicants did a population-based statistical study (1,2) that estimated K1 at 1700. The second population-statistics-based formula that was developed was the correlation of Carbohydrate-to-Insulin Ratio (CIR) by the model: CIR = K2 * Body Weight / TDD.

The model was originally developed by Dr. RD Steed, a colleague of Dr. Davidson in 1998. In 2002 Applicants conducted a statistical study (1,2) that estimated K2 at 2.8, where the Body Weight was measured in pounds. Other authors (3) have referenced these studies as well.

1. Davidson PC, Hebblewhite HR, Bode BW Steed RD, Welch NS, Greenlee MC, Richardson PL, Johnson J. Statistically-Base CSII Parameters: Correction Factor, CF(1700 rule), Carbohydrate-to-Insulin Ratio, CIR (2.8 rule), and Basal-to-Total Ratio. Abstract, Diabetes Technology and Therapeutics 2003, Vol5, #5, pg237
2. Davidson PC, Hebblewhite HR, Bode BW Steed RD, Welch NS, Greenlee MC, Richardson PL, Johnson J, Robertson DG, Supruniuk I, Thomas L Clark JG, Fredrickson L, Van Antwerp W. A Statistically-based Nomogram used as a Teaching Tool for CSII Parameters. Poster 2227, Abstracts of the 18th International Diabetes Federation Congress. Paris , France 24-29 August 2003, Diabetes Metabolism 2003 Aug;29 Spec no 2:4S7-464 * * * can be viewed or copied from wwww.easd.org>IDF Abstracts 2003, Poster Display Sessions>Insulin Therapy Group, Poster # 2227
3. Walsh J, Roberts R, Chandrasekhar V, Bailey T: Using Insulin. San Diego, CA, Torrey Pines Press, 2003

Kaufman et al mention Basal, Bolus, Meal Insulin, Carbohydrate-to-Insulin Ratio (CIR), and Correction Factor (CF) (which they call Insulin Sensitivity) and the well-known bolus formulas: Correction Bolus = (BG-Target)/CF and Meal Bolus = Carbohydrates/CIR. These are discussed in the Background section of Applicants' Specification. Kaufman et al mention fixed formulas for estimating Carbohydrate-to-Insulin Ratio (CIR) and Correction Factor (CF) (their Insulin Sensitivity) that are based on statistical studies of populations. They mention the 1500 Rule. They also mention the 1800 Rule. These formulas are now considered useful only for estimating a starting dosing point after which Applicants adjust these parameters with each use, so the patient is kept up-to-date with a personalized set of parameters. Kaufman et al. do not teach or suggest such adjustment, including for example, adjustment of the parameter CIR itself.

Kaufman et al. also cite the well-known "450 Rule" for Carbohydrate-to-Insulin Ratio (CIR). CIR = 450 / (Total Daily Dose of Insulin) . This is also based on a statistical

analysis of a mean population sample and applies to all patients indiscriminately. It is traditionally used for pump initiation and in special situations where there are no past records and pump therapy must be started from scratch. After that, the usual method is to change CIR and Basal Rate from their previous values with smaller and smaller set adjustments, a process called titration. If fact, the third paragraph of the Kaufman et al.'s section Teaching CSII, at page 344, states that the paragraph is discussing "pump initiation". What further distinguishes Applicant's present disclosure and claims is Applicants automate the titration process, i.e. Applicants calculate new Carbohydrate-to-Insulin Ratio's (CIR's) that are customized to apply to the individual patient and the time-of-day, which is neither taught nor suggested by Kaufman et al.

5. Claim Rejection – 35 USC §102(e)

This rejection is based on the published US patent application to Galley et al. Galley et al., similar to Kaufman, et al., also disclose a population-based statistically derived fixed formula that does not provide for adjustment of insulin dosing departing from the fixed formula, as distinguished from Applicants' disclosure and claims.

Galley et al disclose a formula that employs a curve for "Insulin-on-Board" which is the insulin left active in the body at a given time after dosing. This is an experimentally-determined curve, based on statistical studies of populations and is not exact, since the individual patient may not conform to the population norm. Further, the accuracy of the curve is dependent upon the approach taken by the researchers who determined this curve. Galley et al also disclose a parameter called Insulin Sensitivity, which is the same as Applicants' Correction Factor (CF), but they do not mention a provision for adjusting the CF as Applicants do. They also disclose a parameter called Insulin-to-Carbohydrate Ratio, which is the reciprocal of Applicants' Carbohydrate-to-Insulin Ratio (CIR). They do not, however, teach or suggest a provision for adjusting this parameter as Applicants do. They do further not mention the source of Insulin Sensitivity and Carbohydrate-to-Insulin Ratio; presumably, these two factors are obtained by the physician from population-based statistical studies. In contrast, Applicants adjust their CIR and CF parameters, with no dependence on statistically-correlated results, except one instance in the calculus formula for CIR for an old-vintage pump that has no memory for carbohydrates.

6. Claim Rejections – 35 USC §103(a)

a. Albisser et al. in view of Ribeiro

Albisser, et al dislose an algorithm for subcutaneous pen users. They employ two types of insulin, short-acting and intermediate-acting. They do not use amounts of carbohydrate in the input and do not employ or calculate a Carbohydrate-to-Insulin Ratio (CIR). They do calculate meal insulin doses by means of fixed insulin sensitivity factors (similar to a Correction Factor (CF)), so they depend on the patient eating the same or similar meals every day. Unlike Albisser et al. Applicants disclose and claim Carbohydrate-to-Insulin Ratio (CIR) to calculate the meal insulin, and re-calculate CIR so that dosages are adjusted for the individual patient's needs. Albisser et al use different insulin sensitivity factors (similar to a Correction Factor (CF)) for short and intermediate-acting insulin. These insulin sensitivity factors in fact were fixed for the duration of their study. They state on page 582, "Notably, the sensitivity factors used were fixed for all patients and were never customized for any patient, a process which undoubtedly compromised the speed of dosage adjustment in some." Albisser et al.'s sensitivity factors are also not adjusted for the individual patient's needs.

Ribeiro's algorithm does not provide Basal Rate. In paragraph [0005] he states, "The basal rate is not determined by this invention." By contrast, Applicants not only calculate adjusted Basal Rates for each interval, but insure that the sum of insulin dosing adjustments in an interval meets the requirements indicated by the Corrective Insulin at the interval's end. Ribiero does adjust his Insulin Sensitivity (Applicants' Correction Factor (CF)) but uses a formula based on population statistics, namely the "1800 Rule". One of his main formulas is L = C / ((D – V1)/V5 + D/E). In Applicants' nomenclature, this formula reads, Adjusted CIR = Carbohydrates / ((BG – TargetBG)/CF + BG/CIR). This formula appears throughout. It is fundamentally wrong. The first term in the denominator is in insulin units, but the quantity BG/CIR is in meaningless units. The equation is thus adding apples and oranges in its denominator. The quantity Carbohydrates / CIR would make more sense; in the inventor's nomenclature, this would be C/E, but every instance of this equation in their patent application cites the erroneous equation. But suppose the author were to use an equation having correct units, even so, the correct term, Carbohydrates/CIR (Ribeiro's C/E) only estimates meal insulin.

Applicants allow for this approximation for cases of incomplete data, but prefer to use the actual Meal Insulin injected whenever it is available, since the patient may have second-guessed the formula recommendation and administered a different amount of Meal Insulin. Ribeiro does not account for such a variation. Applicants, on the other hand, given time intervals (for example, about 4 to 8) in which to calculate adjusted CIR's. Ribiero use complicated prior art mathematical techniques from the public domain to interpolate between a small number of values using a polynomial. This is overkill, considering the variability of the typical patient's day. Ribeiro measure the post-meal Blood Glucose (BG) excursions above a Target, cited as 100 mg/dl. This value is the Target used in clinics for pre-meal BG's; the Target for post-meal BG's is normally 140 mg/dl. Ribeiro use post-meal BG's exclusively; the measurement of post-meal BG excursions without taking into account the starting point, i.e. the pre-meal BG is in error. The BG's and Carbohydrates (both input data) appear to be random, but columns of numbers that the author lists for L (output data) increase without decreasing from about 6 to about 15. This makes the algorithm highly suspect. The values of 6 and 15 are not unreasonable for different patients, but such high variation in a single patient is unreasonable.

b. Doyle et al. in view of Galley et al.

Doyle et al. disclose an algorithm that uses a tried-and-true chemical engineering method. However, it deals with Meal Boluses only. It does not address Basal Insulin. It requires two constants to be tuned by human intervention, one constant for the quantity of the Meal Insulin boluses and one for the timing of the bolus. Doyle et al fail to teach or suggest re-calculating these constants within its program with each use, as Applicants do. From a physician's practical point-of-view, if he is going to adjust two parameters from visit to visit, he may as well adjust Basal Rates and CIR, instead of the constants in Doyle et al.'s program.

CONCLUSION

Form the foregoing it can be seen that Applicants' claimed method is novel and not obvious in view of the cited references. Accordingly, favorable action in regard to the application is earnestly solicited. Should the Examiner have any questions regarding this response, the Examiner is invited to telephone the undersigned attorney.

Respectfully submitted ,

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